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EXAMINER	
DUFFY, BRADLEY	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,107	VOLLMERS ET AL.	
	Examiner	Art Unit	
	BRADLEY DUFFY	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-23,27-32,35,47 and 89-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-23,27-32,35,47 and 89-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed June 4, 2009, is acknowledged and has been entered. Claims 21, 27-30, 32, 35, 47 and 96 have been amended.

Priority

2. With regard to the issue of priority, claims 21-23, 27-32, 35, 47 and 89-96 do not properly benefit under 35 U.S.C. §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since those claims are remain rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under 35 USC §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Furthermore, claims 21-23, 27-32, 35, 47 and 89-96 do not properly benefit by the earlier filing because, because the prior applications do not contain written support for the claims for the reasons set forth in the below rejection of the instant claims as containing NEW MATTER.

Accordingly, the effective filing date of the claims is deemed the filing date of PCT/IB04/04453, namely November 12, 2004.

Grounds of Objection and Rejection Withdrawn

3. Unless specifically reiterated below, Applicant's amendment and/or arguments filed June 4, 2009, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed July 25, 2008.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The rejection of claims 21-23, 27-32, 35, 47 and 89-96 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained.

At page 8 of the amendment filed June 4, 2009, Applicant has traversed this ground of rejection, arguing that the term "functional fragment" is definite because the claims recite "binds" and therefore one of skill in the art would understand that the function referred to by "functional fragment" is binding.

In response, while the "functional fragment" must specifically bind an epitope, as set forth in the previous office action, this recitation of "functional fragment" renders the claim indefinite because antibodies are known to have multiple functions and it is unclear to which function is being referring to. In this case, based on Applicant's response, it appears that Applicant intends the fragment to be an antigen-binding fragment, so it is suggested that the claims be amended to recite "antigen-binding fragment" instead of "functional fragment" to obviate this rejection.

For these reasons, after careful and complete consideration, it is maintained that these claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. The rejection of claims 21-23, 27-32, 35, 47 and 89-96 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

Starting at page 13 of the amendment filed June 4, 2009, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

Again, the considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description'' Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

In the instant case, the claims remain drawn to a structurally and functionally diverse genus of "antibodies or functional fragments thereof", such as an antibody comprising a heavy chain variable region with at least 80% identity to SEQ ID NO:5 and that includes amino acids 99-108 of SEQ ID NO:5 and a light chain variable region with at least 80% identity to the amino acid sequence of SEQ ID NO:7, wherein the antibody or functional fragment specifically binds to an epitope of: antigen expressed by at least one of Colo-699 (DSMZ Accession Number ACC 196), CACO-2 (DSMZ Accession Number ACC 169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU-145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), and BM 1604 (DSMZ Accession Number ACC 298) cells, wherein NORM-2 antibody produced by a cell line deposited as DSM ACC 2626 (see claim 21) or an antibody comprising amino acids 31-35, 50-66, and 99-108 of SEQ ID NO:5 or amino acids 23-36, 52-58, and 91-101 of SEQ ID NO:7 or a functional fragment thereof wherein the antibody or functional fragment specifically binds to an epitope of: antigen expressed by at least one of Colo-699 (DSMZ Accession Number ACC 196), CACO-2

(DSMZ Accession Number ACC 169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU-145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), and BM 1604 (DSMZ Accession Number ACC 298) cells, wherein NORM-2 antibody produced by a cell line deposited as DSM ACC 2626 (see claim 27). Further dependent claims set forth other percent identities that the antibody must have when compared to SEQ ID NOs:5 and/or 7 (see claims 22, 23, 89, 90, 91 and 92), that the antibody or functional fragment thereof induces apoptosis (claim 93) or decreases proliferation (claim 94) of any one of Colo-699 (DSMZ Accession Number ACC 196), CACO-2 (DSMZ Accession Number ACC169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU- 145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), or BM 1604 (DSMZ Accession Number ACC 298) cells, or that the heavy or light chain variable region has an insertion, deletion or substitution in one amino acid residue in either or both of SEQ ID NO:5 and SEQ ID NO:7. In this case, the claims as amended do not require that the antibodies specifically bind to any particular antigen or necessarily comprise each of the 6 complementarity determining regions (CDRs) of the monoclonal antibody Norm-2, i.e., the CDRs[1] that are disclosed in the heavy chain variable domain of SEQ ID NO:5 and the light chain variable region of SEQ ID NO:7, wherein the antibody specifically binds the same antigen as the Norm-2 antibody produced by the cell line deposited as DSMZ accession number DSM ACC2626, nor do the claims require that the fragment be an antigen-binding fragment comprising each of the 6 complementarity determining regions (CDRs) of the monoclonal antibody Norm-2, i.e., the CDRs that are disclosed in the heavy chain variable domain of SEQ ID NO:5 and the light chain variable region of SEQ ID NO:7, wherein the antigen-binding fragment specifically binds the same antigen as the Norm-2 antibody produced by the cell line deposited as DSMZ accession number DSM ACC2626.

Starting at page 13 of the response filed June 4, 2009, it appears that Applicant is arguing that the Norm-2 antibody species disclosed in the specification is

[1] See page 3 of the specification for a disclosure of the CDR sequences present in SEQ ID NO:5 and 7

representative of the genus of claimed antibodies which, as set forth above, need not bind to any particular well-characterized antigen and which need not comprise 6 complementarity determining regions (CDRs) because the skilled artisan has substantial understanding of antibody structure and function and because the specification identifies the 6 CDRs of the monoclonal antibody Norm-2.

In response, this argument is first not found persuasive because the recited cell lines which must be bound by the claimed antibody "variants" express multiple different antigens and the specification has not identified or characterized the antigen to which the monoclonal antibody designated Norm-2 specifically binds and therefore it is apparent that the claims are not directed to antibodies that specifically bind to a well-characterized antigen.

Secondly, this argument is not found persuasive because while the Examiner acknowledges that the skilled artisan is aware of well-known and conventional methodologies for producing monoclonal antibodies that bind the same antigen as a parent antibody by CDR grafting heavy and light chain CDRs into corresponding heavy and light chain frameworks to give an antibody that binds the same antigen as the parent antibody, the Examiner respectfully disagrees that the understanding of antibody structure and function in the art at the time of filing was sufficient for one of skill in the art to immediately envision the antigen bound by the antibody "variants" encompassed by the claim or the antibody variants comprising less than all 6 CDRs in the proper context of variable light and heavy chain domains which would bind the same antigen as the monoclonal antibody designated Norm-2 produced by a cell line having a deposit number of DSM ACC2626. In this case, while Applicant has identified art suggesting that for particular antibodies specific for some particular epitopes on some particular antigens, that functionally active peptides comprising less than all 6 CDRs of an antibody in their proper context of antibody framework regions might be obtained, this evidence does not establish that one of skill in the art could immediately envision which framework amino acid positions or which CDR amino acid positions can be predictably altered to produce a variant which retains antigen-binding properties of the parent

antibody. As set forth in the previous action, one of skill in the art recognizes that the effect of even one amino acid change is highly unpredictably on antigen-binding function and therefore it is maintained that one of skill in the art would not find the Norm-2 antibody species representative of antibodies that need not bind the same antigen as the parent antibody and which need not comprise a heavy chain variable region comprising the three heavy chain CDRs of the monoclonal antibody designated Norm-2 produced by a cell line having a deposit number of DSM ACC2626 and a light chain variable region comprising the three light chain CDRs of the monoclonal antibody designated Norm-2 produced by a cell line having a deposit number of DSM ACC2626. In this case, other than identifying the CDRs of the NORM2 antibody, the specification does not further characterize which amino acids of the monoclonal antibody designated Norm-2 produced by a cell line having a deposit number of DSM ACC2626 are required for antigen-binding and therefore one of skill in the art could not envision which amino acids should be retained for antigen binding and which could be altered while retaining antigen binding. Accordingly, the claims do not require that the antibodies or fragments thereof comprise the particularly identifying structural features, i.e., all 6 CDRs in their proper context, of the monoclonal antibody designated Norm-2 produced by a cell line having a deposit number of DSM ACC2626 which correlates which its antigen-binding function. Notably, while the antibodies or fragments need now include amino acids 99-108 of SEQ ID NO:5, which is the sequence of one of the CDRs, the claims do not set forth that the antibodies need comprise these amino acids as a CDR sequence so it is further apparent the claims need not comprise the particularly identifying structural features of the monoclonal antibody designated Norm-2 produced by a cell line having a deposit number of DSM ACC2626. Applicant is reminded, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Thus, although the skilled artisan might be able to screen for other antibodies or fragments thereof to determine if antibodies or fragments thereof with the recited structures and functions encompassed by the claims *exist*, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement

provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for identifying it.

Thus for these reasons and the reasons set forth in the previous office action it is maintained that the specification only adequately describes isolated antibodies or antigen-binding fragments thereof, wherein the antibody or antigen-binding fragment thereof specifically binds the same antigen as the monoclonal antibody produced by the cell line deposited as DSMZ accession number DSM ACC2626, and wherein said antibody or said antigen-binding fragment thereof comprises: a heavy chain variable domain comprising a CDR1 comprising the amino acid sequence of amino acids 31-35 of SEQ ID NO:5, a CDR2 comprising the amino acid sequence of amino acids 50-66 of SEQ ID NO:5 and a CDR3 comprising the amino acid sequence of amino acids 99-108 of SEQ ID NO:5 and a light chain variable domain comprising a CDR1 comprising the amino acid sequence of amino acids 23-36 of SEQ ID NO:7, a CDR2 comprising the amino acid sequence of amino acids 52-58 of SEQ ID NO:7 and a CDR3 comprising the amino acid sequence of amino acids 91-101 of SEQ ID NO:7.

In summary, after careful and complete consideration of Applicant's arguments, for these reasons and as explained more fully in the Office action mailed July 25, 2008, the specification as filed would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed and this rejection is maintained.

8. The rejection of claims 21-23, 27-32, 35, 47 and 89-96 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** isolated antibodies or antigen-binding fragments thereof, wherein the antibody or antigen-binding fragment thereof specifically binds the same antigen as the monoclonal antibody produced by the cell line deposited as DSMZ accession number DSM ACC2626, and wherein said antibody or said antigen-binding fragment thereof comprises: a heavy chain variable domain comprising a CDR1 comprising the amino acid sequence of amino acids 31-35 of SEQ ID NO:5, a CDR2 comprising the amino acid sequence of amino acids 50-66 of SEQ ID NO:5 and a CDR3 comprising the amino

acid sequence of amino acids 99-108 of SEQ ID NO:5 and a light chain variable domain comprising a CDR1 comprising the amino acid sequence of amino acids 23-36 of SEQ ID NO:7, a CDR2 comprising the amino acid sequence of amino acids 52-58 of SEQ ID NO:7 and a CDR3 comprising the amino acid sequence of amino acids 91-101 of SEQ ID NO:7, *provided* the deposit requirements are first met for the cell line deposited as DSMZ accession number DSM ACC2626, **and while being enabling for making and using** any antibodies or functional fragments thereof encompassed by the claims, which have been described by the prior art, **does not reasonably provide enablement for making and using** the full scope of the claimed antibodies and functional fragments thereof, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Starting at page 8 of the amendment filed June 4, 2009, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

In the traversal, Applicant has first argued that the cell lines Colo-699 (DSMZ Accession Number ACC 196), CACO-2 (DSMZ Accession Number ACC169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU-145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), or BM 1604 (DSMZ Accession Number ACC 298) recited in the claims are publicly available and

has provided Exhibit E which details information sheets describing the recited cell lines from the DSMZ catalog.

In response, this Exhibit is insufficient to establish the public availability of the recited cell lines. Notably, the supplied information sheets do not establish that any of the recited cells lines are publicly available or when the cell lines were deposited or made publicly available.

Secondly, with respect to the cell line deposited as DSMZ accession number DSM ACC2626 which produces a monoclonal antibody designated NORM-2 at page 9 Applicant avers that due to the propriety nature of the deposit it would be premature to make assurances that the cell line deposited as DSMZ accession number DSM ACC2626, which was deposited under the provisions of the Budapest Treaty, will be replaced if viable samples cannot be dispensed by the depository, that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application and access to the deposit will be available during pendency of the patent application making reference to the deposit to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 U.S.C. 122.

In response, the necessary declaration does not require that the material be made immediately publicly available. It will only become publicly available upon the grant of a patent. Therefore, it is not premature to make the assurances and in the absence of such assurances the rejection will be properly maintained.

Finally, it appears that Applicant has argued that the claimed antibodies and fragments thereof are enabled because one of skill in the art could screen for antibodies or fragments thereof as encompassed by the claims using methods set forth in the specification and because one of skill recognizes that it is routine and conventional to make antigen binding variants of a parent antibody comprising deletions or substitutions such that the variant comprises less than all 6 CDRs of a parent antibody (see response at page 9 and 11 in particular).

In response, this argument is not found persuasive because the Examiner respectfully disagrees that it was routine or conventional in the art to make antibodies

comprising less than all 6 CDRs that are functionally equivalent to a parent antibody. While Applicant has identified art suggesting for particular antibodies specific for some particular epitopes on some particular antigens, that functionally active fragments comprising less than all 6 CDRs of an antibody in their proper context of antibody framework regions might be obtained, it has not been established that it is conventional or routine in the art to be able to make such fragments for *any and every* given parental antibody and the instant specification does not provide any specific, non-general guidance which would allow one of skill in the art to make and use the full scope of the claimed antibodies. Notably, in this case, the specification does not make any such variants and does not identify any particular CDR resides which might be varied to make an antibody or fragment thereof with different CDR sequences which retains the functions of the parent antibody.

Additionally, this argument is not found persuasive because although one could potentially screen antibody libraries that comprise the recited sequences with random CDRs or randomly mutated CDRs at the other CDR positions to identify those antibodies that comprise functional equivalents of the CDRs of the parental antibody the specifically binds the same antigen as the parent antibody, the artisan cannot predict whether any given CDR will function in a manner complementary to a corresponding CDR present in the parental antibody. The functionality of candidate CDRs can only be determined empirically. Because *it cannot be known beforehand* whether in fact there are functional equivalents of the CDRs of the parental antibody that specifically binds the same antigen, which can be used to produce the claimed antibodies with less than all 6 of the CDRs present in the parental antibody which specifically binds the same antigen, it is submitted that the production of the claimed invention by the artisan would fall into the realm of undue and/or unreasonable experimentation, despite the routine nature of the screening process itself by which such functional equivalents might, if such exist, be identified. Accordingly undue and unreasonable experimentation would be required to determine which CDRs could predictably be altered or substituted while retaining antigen-binding function.

It should be further noted that the claims do not require that the antibody even bind the same antigen as the monoclonal antibody produced by the cell line deposited as DSMZ accession number DSM ACC2626. Accordingly, one of skill in the art would also be subject to undue and unreasonable experimentation to identify uses for the antibodies which bind to the entire genus of antigens encompassed by the claims.

Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997).

Thus, the overly broad scope of the claims would merely serve as an invitation to one skilled in the art to identify other antibodies that are encompassed by the claims; yet, defining a substance by its principal biological activity amounts to an alleged conception having no more specificity than that of a wish to know the identity of any material with that biological property. See *Colbert v. Lofdahl*, 21 USPQ2d 1068, 1071 (BPAI 1991).

In conclusion, upon careful and full consideration of Applicant's arguments and the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enabled the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation, and this rejection is being maintained.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. The rejection of claims 21, 27, 30, 31, 47 and 95 under 35 U.S.C. 102(b), as being anticipated by Immunobiology 5 (Edited by Janeway et al, pages 96-97, 2001) as evidenced by Kettunen et al (C. Gen. Cyto., 149:98-106, 2004), is maintained.

The claims are herein interpreted as being drawn to a functional fragment of an antibody, such as an Fc fragment. Notably, at page 9 of the specification examples of functional fragments are taught which include an Fc fragments. Furthermore, since Fc fragments do not comprise variable domains comprising, e.g., the variable domain sequences of SEQ ID NO:5 and/or SEQ ID NO:7, it is apparent that the functional fragments recited in claim 21 and 27 should be broadly, but reasonably interpreted to include functional fragments that do not comprise any of the recited variable domain sequences, such as an Fc fragment. This is in contrast to other claims that are not included in this rejection, which recite wherein clauses that limit the functional fragment to comprise some part of the amino acid sequence of SEQ ID NO:5 and/or 7 (see e.g., claim 22 which recites the phrase "wherein said polypeptide antibody or a functional fragment thereof comprises a heavy chain variable region with at least 85% identity to the amino acid sequence of SEQ ID NO:5". Furthermore, claim 47 is being included in this rejection because Fc fragments could be obtained from the recited cell line which produces a monoclonal antibody as well as producing numerous polypeptides. Finally, claim 21 requires that the functional fragment thereof specifically bind to a cell line such as the lung adenocarcinoma designated Colo-699. Notably, as evidenced by Kettunen et al, adenocarcinomas of the lung express the Fc receptor, FcRn, and this receptor specifically binds to the Fc domain of IgG antibodies.

At page 19 of the response filed June 4, 2009, Applicant has traversed this ground of rejection.

In this response, Applicant has argued that Immunobiology 5 does not teach binding to the recited cell lines such as the lung adenocarcinoma designated Colo-699.

In response, while Immunobiology 5 does not test the Fc region for binding to the lung adenocarcinoma cell line designated Colo-699, as evidenced by Kettunen et al in the previous office action the Fc fragment inherently has this function. Furthermore, the Office lacks the resources and facilities to compare the Fc fragment disclosed by the prior art and the Fc fragment as encompassed by the instant claims to establish whether there are any differences. Consequently, in the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed Fc fragment is different than that taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977); and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

For these reasons and as further explained in the previous Office action, and after careful and complete consideration of Applicant's response, this rejection is being maintained.

11. The rejection of claims 21-23, 27-31, 35, 47 and 89-96 under 35 U.S.C. 102(b), as being anticipated by Vollmers et al (Cell, 40:547-557, 1985, IDS filed 3/16/2007), is maintained.

At page 20 of the response filed June 4, 2009, Applicant has traversed this ground of rejection.

In this response, Applicant has argued the rejection is contradictory to the enablement rejection of the claims and argued that there is no information in Vollmers indicating that their antibody is publicly available so the Vollmer antibody is not enabled.

In response, the rejections are not contradictory because the enablement rejection is a scope of enablement rejection and the standard of enablement for a prior art reference is different than the standard of enablement of a pending application. With respect to the enablement of Vollmers as set forth in MPEP 2121:

> When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07.

Accordingly, Applicant's arguments about the availability of the antibody of Vollmers are insufficient because no evidence has been presented which establishes that the antibody of Vollmer was not publicly available. For example, as a requirement of publication researchers may be required to make reagents available to those that request it, so lack of an express statement that the antibody is publicly available in Vollmers is insufficient to establish that the Vollmers antibody is not operable. Once again, the Vollmers antibody is presumed to be operable and the burden is on applicant to provide facts rebutting the presumption of operability. Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, *inoperability of the prior art*, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

For these reasons and as further explained in the previous Office action, and after careful and complete consideration of Applicant's response, this rejection is being maintained.

12. The rejection of claims 21-23, 27-31, 35, 47 and 89-96 are rejected under 35 U.S.C. 102(a) as being anticipated by Brandlein et al (Can., Res., 7995-8005, 2003, IDS filed 3/16/2007), is maintained.

At page 21 of the response filed June 4, 2009, Applicant has traversed this ground of rejection.

In this response, Applicant has argued that the rejection should be withdrawn because the instant claims have a priority date of 11/12/2003.

In response, for the reasons set forth in the priority section above the effective filing date of the claims is deemed November 12, 2004.

Accordingly, for this reason and as further explained in the previous Office action, and after careful and complete consideration of Applicant's response, this rejection is being maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 21-23, 27-32, 35, 47 and 89-96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21-23, 27-32, 35, 47 and 89-96 are indefinite because they have been amended to recite, "wherein NORM-2 antibody produced by a cell line deposited as DSM ACC 2626 specifically binds to *said epitope of the antigen* expressed by at least one of Colo-699 (DSMZ Accession Number ACC 196), CACO-2 (DSMZ Accession Number ACC 169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU- 145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), and BM 1604 (DSMZ Accession Number ACC 298) cells an adenocarcinoma of the colon, a diffuse type". Notably, while the claims set froth that the antibody or fragment binds an epitope of an antigen expressed by one of the recited cell lines, because the recited cell lines express many antigens comprising many epitopes, the limitation *said epitope* lacks proper antecedent basis and it is unclear to which epitope of an antigen expressed by the recited cell lines is being referred to. Thus, the claims fail to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled artisan

to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 21-23, 27-32, 35, 47 and 89-96 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

In this case, claim 21 recites the new limitation "and that includes amino acids 99-108 of SEQ ID NO:5" and claims 21, 27 and 96 also recite the new limitation "wherein the antibody or functional fragment thereof specifically binds to an epitope of an antigen expressed by at least one of Colo-699 (DSMZ Accession Number ACC 196), CACO- 2 (DSMZ Accession Number ACC 169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU-145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), and BM 1604 (DSMZ Accession Number ACC 298) cells, wherein NORM-2 antibody produced by a cell line deposited as DSM ACC 2626 specifically binds to said epitope of the antigen expressed by at least one of Colo-699 (DSMZ Accession Number ACC 196), CACO-2 (DSMZ Accession Number ACC 169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU- 145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), and BM 1604 (DSMZ Accession Number ACC 298)."

At page 7 of the response filed June 4, 2009, Applicant has indicated that support for "the amendment to claim 21 to recite a heavy chain variable region "that includes amino acids 99-108 of SEQ ID NO:5" is supported, for example, at page 3,

lines 5-12, at page 10, lines 5-11, at page 14, lines 5-12, and at page 48, line 19, to page 49, line 7" and that "[t]he amendment to claims 21, 27 and 96 to recite that the antibody or functional fragment thereof "specifically binds to an epitope of an antigen expressed by at least one of" the recited cell lines, and "wherein NORM-2 antibody produced by a cell line deposited as DSM ACC 2626 specifically binds to said epitope of the antigen expressed by at least one off the recited cell lines is supported, for example, at page 1, lines 27-28, which discloses "a class of polypeptides which react with epitopes specific for neoplastic cells," at page 18, lines 22-25, which discloses "two monoclonal antibodies (NORM- 1 and NORM-2)....that specifically recognize a number of carcinomas"

Contrary to Applicant's assertion, however, it does not appear that the specification, including the claims, as originally filed, provides written support for the language of the claims.

In this case, while the specification at page 10, lines 5-11, sets forth that a functional fragment may comprise amino acids 31-35, 50-66, and/or 99-108 of SEQ ID NO:5, support for the claimed antibodies comprising this amino acid sequence in combination with the percent identity language set forth in the claims could not be found in the specification as filed. Notably, while page 14, lines 4-10 sets forth that polypeptides of the invention can have 80%, 85%, 90%, or 95% identity to a reference amino acid sequence, the specification does not appear to set forth antibodies comprising amino acids 99-108 of SEQ ID NO:5 in combination with antibodies having the percent identity language set forth in the claims.

Additionally, with respect to the other new limitation it is noted that the cell lines designated Colo-699 (DSMZ Accession Number ACC 196), CACO- 2 (DSMZ Accession Number ACC 169, ATCC Accession Number HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU-145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), and BM 1604 (DSMZ Accession Number ACC 298) express multiple structurally and functionally different antigens as discussed supra. However, the specification does not identify that the NORM-2 antibody produced by a cell line deposited as DSM ACC 2626 can bind such structurally and functionally different

antigens expressed by these cell lines, so it is submitted that given the apparent difference in the breadth of the claims and that of the pertinent disclosures it is submitted that this clearly illustrates that such amendments have in fact introduced new concepts, thereby violating the written description requirement set forth under 35 U.S.C. §112, first paragraph.

Applicant is reminded that it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See *In re Smith*, 173 USPQ 679, 683 (CCPA 1972).

Otherwise these issues might be resolved if Applicant were to point to other disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary written support for the language of the instant claims.

Conclusion

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571)272-9935. The examiner can normally be reached on 7-4:30 M-F with alternate Fridays off, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

/bd/
Examiner, Art Unit 1643
August 26, 2009